40th Annual NCDEU Meeting: AGENDA

(Schedule is tentative and subject to change; will be updated regularly)

Monday, May 29

8:30 AM – 5:00 PM **New Investigators' Workshop** (*closed session*)

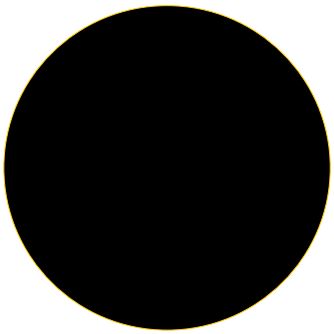
Leaders:

Mark Rapaport, M.D., University of California, San Diego
Barry Lebowitz, Ph.D., National Institute of Mental Health

The New Investigator's Program began in 1992 and has brought between 16-20 new investigators to the NCDEU meeting. This 1-day closed-session workshop, targeted toward junior investigators in the field of psychopharmacology will give then the opportunity to present their posters at the NCDEU poster sessions, and be recognized at a special reception given in their honor. The vast majority of Awardees have continued to work in the public, academic, or private sectors of psychopharmacology.

The objectives of this workshop are:

1) To examine the general principles of treatment research
2) To critically discuss the various types of clinical trials, and the methodological/statistical considerations of each
3) To explain approaches and opportunities for grant application from NIH and other sources



Tuesday, May 30

Workshops:

8:30 AM – 4:00 PM **Enhancing Precision in Clinical Trials III**

This workshop is a forum for the critical review of ideas and techniques for enhancing precision in treatment research. This is designed to be an interactive meeting where the audience actively participates in the evaluation of material presented. The presentations should serve as a stimulus for discussion and new suggestions about trial design approaches.

The objectives of this workshop are:

1. To identify new data about attempts to enhance precision in treatment research.
2. To examine new techniques and technologies that may enhance precision.
3. To identify original theoretical approaches that may influence the future design of treatment trials.

9:00 AM – 5:00 PM **Methodological Challenges in Pediatric Clinical Trials**

This workshop will address common challenges in designing clinical trials in youth. With awareness that decisions must be based on the specific aims of each individual study, the workshop will offer examples of commonly encountered situations in pediatric treatment research, as a stimulus for a more general debate on study designs and methods.

The objectives for this workshop are:

1) To examine the choice of valid, sensitive, and easily interpretable outcome measures;
2) To identify the selection of the primary raters of the treatment outcome
3) To define the relevant, informative, and ethical control and comparison groups
4) To examine the methodology for studying the cost/effectiveness of treatments.

9:00-12:00 noon **Part A:** *Which Outcome Measures? Which Raters? Which Control/Comparison Groups?*

Leaders: Katharine Phillips, M.D. and Benedetto Vitiello, M.D.

- **Selecting the Primary Dependent Variable(s): Multiple Variables vs. Overall Outcome**

  Presenter: Peter S. Jensen, M.D., Columbia University

  Discussants: Nina Schooler, Ph.D., Hillside Hospital, North Shore LIJ Health System

  Andrew C. Leon, Ph.D., Cornell University

- **Choosing the Primary Raters of Treatment Outcome**

  Presenter: Graham Emslie, M.D., U. of Texas, Southwestern Med. Center

  Discussant: Thomas Spencer, M.D., Harvard Medical School

- **Treatment as Usual: The MTA Experience**

  Presenter: Laurence Greenhill, M.D., Columbia University

  Discussant: Mark Riddle, M.D., Johns Hopkins University

The Statistician's Comments: Michael Borenstein, Ph.D., Hillside Hospital, North Shore LIJ Health System

1:30-5:00 pm **Part B:** *Assessing Cost-Effectiveness of Treatment Interventions*

Leaders: Kimberly Hoagwood, Ph.D. & Benedetto Vitiello, M.D.

Approaches to conducting cost/benefit analyses in child psychiatric clinical trials will be presented and discussed.

Presenters:

Gregory Clarke, Ph.D., Kaiser Permanente
Frances Lynch, Ph.D., Kaiser Permanente
Nancy Wolff, Ph.D., Rutgers University
Pinka Chatterji, Ph.D., Columbia University
Jeff Hoch, Ph.D., University of Western Ontario

9:00 AM – 12:00 Noon **Magnetic Resonance Imaging: What's Feasible and What's Needed?**

Leaders: **Michael Henry, MD**, *McLean Hospital*
Mark Schmidt, MD, *Eli Lilly & Co*

- **Proton Spectroscopy in Dementia**
  P. Murali Doriswami, Duke University

- **Using Spectroscopy To Measure Brain Drug Levels**
  Michael Henry, M.D., McLean Hospital

- **fMRI and Drug Effects**
  Perry Renshaw or Debbie Yurgelun-Todd.

- **How Does the FDA view such Data**
  Paul Andreasen, MD, Food and Drug Administration

- **Can MRI Be Used To Augment Pre-clinical Models**

- **MRI And Clinical Trials**
  Mark Schmidt, Eli Lilly, Co.

The objectives of this workshop are:

1) To define modern brain imaging approaches used in the study of mental disorders and their treatments
2) To identify the role of brain imaging in the medication development process, including scientific and regulatory implications

2:00 PM – 5:00 PM **Meeting the Operational Challenge: The NIMH Initiative for Multicenter Clinical Trials**

Chairs: Leslie Leahy, Ph.D., Massachusetts General Hospital
Stephen Wisniewski, Ph.D., University of Pittsburgh

The objectives for this panel session are:

1. To describe the start-up process for initiating large-scale clinical trials
   the roles of professional and support staff in the recruitment, screening, treatment, and assessment processes of clinical trials
2. To critically discuss present recommendations for successful interactions between clinical investigators and internal and external oversight review and data safety monitoring boards

2:00 PM – 5:00 PM **Translating Substance Abuse Treatment Research to Practice: Innovative Trial Designs**

In recent years, clinical trials, which go beyond establishing safety and efficacy, have received increased attention. These types of studies focus on developing information to assist clinicians in typical community practice on the most appropriate ways to use a medication. In this workshop, presentations on several late phase III or phase IV studies will be made to illustrate the types of issues to be considered in designing these studies. The Director of NIDA's Division of Treatment Research and Development will discuss this area from the perspective of the NIDA Medication Development Program. Also, a representative of FDA's Division of Anesthetic, Critical Care & Addiction Drug Products, Center for Drug Evaluation and Research will discuss the FDA perspective on what types of trials support regulatory decision-making and labeling, and what types of trials offer information relevant to the art and practice of medicine.

Chairs: Jack Blaine, MD, National Institute on Drug Abuse
Barbara Mason, PhD, University of Miami

Presenters: Frank Vocci, PhD, National Institute on Drug Abuse
Ann Montgomery, RN, National Institute on Drug Abuse
Robert Walsh, National Institute on Drug Abuse
Celia Winchell, Food and Drug Administration

The objectives of this workshop are:

1. Examine the special challenges associated with clinical research in a substance abusing population, including issues of comorbid mental and physical disorders and treatment adherence
2. Discuss critically the current and planned intervention studies and new approaches to studying novel treatments of alcohol, opiate, and cocaine abuse

Open Forum:

4:00 PM – 6:00 PM **The Future of Psychopharmacology:**
Generativity and Mentoring

Presenter: **Ira Glick, M.D., Stanford University**

This open forum is designed to begin thoughtful discussion about generativity and mentorship. Some of the issues to be addressed include:

1. How do we develop into mentors?
2. What are the components of mentorship?
3. In evaluating successful mentors and mentorship programs, are there certain common themes that develop? What role does generativity play in mentorship?
4. How is the complicated transition in relationship from mentor-mentee to colleagues navigated?

The objectives for this open forum are:

1. To examine and present for discussion the concept of mentorship.
2. Define key components of mentorship.
3. Describe critically the dynamic nature of the mentor-mentee relationship.

7:00 PM **Evening: New Investigators' Reception (Open)**

Wednesday, May 31

8:30 AM – 9:00 AM Welcome from NIMH

9:00 AM – 12:00 Noon **Plenary Session:** ***The First Half-Century of Psychopharmacology Research: A Look Back, the Vision Ahead***

Presenters: Jonathan Cole, M.D., *McLean Hospital*

Husseini Manji, M.D., *Wayne State University*

Steven Hyman, M.D., *National Institute of Mental Health*

The objectives for this plenary session are:

1) Describe the history of the field of psychopharmacology
2) Examine how advances in treatment of mental disorders have led to advances in new drug development
3) Explain how new knowledge in the genetics of mental disorders and drug metabolism are leading to new research approaches for the study of mental disorders and their treatment

12:30 PM – 2:00 PM **Poster Session I:** *(posters will remain up until 6:00 PM)*

2:00 PM – 3:30 PM **Update Session I:**

Race and Mood Disorders

Presenter:

William Lawson, MD, PhD, *Roudebush VA Medical Center, Indianapolis*

Objectives:

1. Examine the role of race as an important variable in understanding psychiatric diagnosis, treatment approach, and treatment response
2. Define new findings in pharmacogenetics that may enhance treatment of mental disorders in various ethnic populations

Reflections of Public Participation in the Mental Health Research Process

Presenter:

Mr. James McNulty, *National Alliance for the Mentally Ill*

Objectives:

1. To examine and illustrate the new role of patients / consumers in the review process for NIH grant applications
2. Discuss critically the implications of public participation in the generation of research plans and in the informed consent process

Translational Research

Presenter:

Dennis Charney, MD, *Yale University*

The objectives for this update session are:

1. Examine the process of converting a theoretical or laboratory finding into a clinical study
2. Illustrate from the fields of anxiety and mood disorders research, to demonstrate how knowledge gained from the study of stress response may be adapted to further our understanding of the pathophysiology of depression and post-traumatic stress disorder

Panels (Concurrent):

3:45 PM – 5:15 PM

Panel 1: Practice Guidelines, Treatment Algorithms: Will They Really Change Practice?

Chair: Junius Gonzales, MD, National Institute of Mental Health

The objectives for this panel are:

1. Identify current endeavors in practice guidelines, treatment algorithms, and dissemination/implementation efforts.
2. Examine why providers don't apply practice guidelines.
3. Discuss critically the approaches to successfully implementation of practice guidelines and algorithms.

A. Presentations

1. Texas Medication Algorithm Project (TMAP)
   Dr. Madhukar Trivedi 3:45-4:05

   Goal: to understand the development and implementation of the TMAP and its relevance to day to day practice

2. American Psychiatric Association/NY State Project
   Dr. Joyce West 4:05-4:25

Goal: to hear the approach and results of this implementation study with practicing psychiatrists

3. Implementing AHCPR Depression Guidelines in a Primary Care IPA
Dr. Junius Gonzales 4:25-4:45

Goal: to understand the role of academic detailing and structural barriers in this randomized trial of implementing guidelines

B. Commentary:

Why Guidelines Aren't Used
Dr. Michael Cabana 4:45-5:05

Goal: to understand the broader conceptual issues in why providers may not use guidelines

C. Questions 5:05-5:15

3:45 PM – 5:15 PM

Panel 2: Drug-Drug and Drug-Herb Interactions: From CYPs to Gene Chips

Chair: Cara Alfaro, Pharm.D, *National Institutes of Health*

The objectives for this panel are:

- Describe updated information and clinical implications of Cytochrome P450 Isoenzyme inhibition and/or induction as it relates to psychotropic medications
- Identify Cytochrome P450 Isoenzyme inhibition and induction properties of several herbal preparations and potential interactions with prescribed medications.
- Recognize the benefits and limitations of Cytochrome P450 gene chip technology in the clinical management of patients.

Advances in Psychotropic CYP Interactions

Larry Ereshefsky, Pharm.D.

The University of Texas Health Science Center at San Antonio and The University of Texas at Austin College of Pharmacy

Drug - Herb Interactions

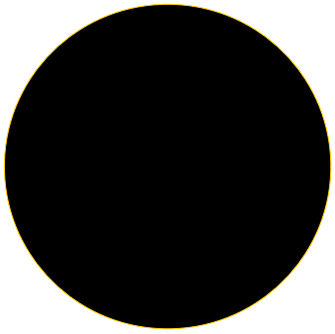
Cara Alfaro, Pharm.D, National Institutes of Health

CYP Phenotype and Genotype: Evolution of Gene Chip Technology in Clinical Practice

David Flockhart, MD, Ph.D.; Georgetown University

General Discussion

7:00 PM **Evening: NIMH Reception (Open)**



Thursday, June 1

7:00 AM

2nd Annual Fun Run / Walk (separate registration required)

Morning Panels (Concurrent):

9:00 AM – 10:30 AM

Panel 3: NIMH Large-Scale Adult and Geriatric Clinical Trials

Chair: Barry Lebowitz, Ph.D., National Institute of Mental Health

Presenters:

Jeffrey Lieberman, M.D., University of North Carolina
A. John Rush, M.D., University of Texas Southwestern Medical Center at Dallas
Gary Sachs, M.D., Massachusetts General Hospital
Lon Schneider, M.D., University of Southern California

The objectives for this panel session are:

1. To define the goals and challenges of *efficacy* versus *effectiveness* treatment research
2. To examine several new NIMH multi-site trials in the areas of bipolar disorder, treatment-resistant depression, and the use of atypical antipsychotics in the treatment of schizophrenia and Alzheimer's Disease, with an emphasis on methodological considerations

9:00 AM – 10:30 AM

Panel 4: Health Risks of Antipsychotic Medication and the Possible Relation to Clinical Response

Presenters:

Robert L. Dufresne, Pharm.D. Charles Caley, Pharm.D. and Jonathan Lacro, Pharm.D.

The objectives for this panel session are:

Atypical Antipsychotics: Effects on Weight and Serum Lipids

1. To describe how serum lipid levels are affected by both typical and atypical antipsychotics.
2. To examine the relation between the use of typical and atypical antipsychotics and weight gain.
3. To identify the best ways to manage these problems in their patients on antipsychotics.

Serum Lipids and Response in Schizophrenia and Affective Disorders

1. To examine the current literature pertaining to the relationship between serum lipids and psychiatric psychopathology
2. To examine the relationship between serum lipids and response to pharmacotherapy in patients with schizophrenia and affective disorders.
3. To relate the changes in serotonergic and dopaminergic systems by medication with serum lipids

Cardiovascular Co-morbidity and Schizophrenia

1. To describe the various effects of antipsychotic treatment on cardiovascular functioning in schizophrenic patients.
2. To identify how to modify therapy in such patients.
3. To analyze the relationship between changes in serum lipids, weight, and other antipsychotic effects and co-morbid cardiovascular pathology.

10:45 AM – 12:15 PM **Update Session II:**

A Screening Tool for Bipolar Disorder: Finally

Presenter:

Robert Hirschfeld, MD, *University of Texas Medical Branch at Galveston*

The objectives for this update session are:

1. To review the history and application of screening questionnaires and structured interviews in mood disorder research
2. To present data supporting the validity and reliability of a new screening tool for the diagnosis of hypomania and its application in clinical research

Developmental Neurobiology and the Etiology of Schizophrenia

Presenter:

Douglas Meinecke, PhD, *National Institute of Mental Health*

The objectives for this update session are:

1. To examine the theories and supporting data relating early brain insult to the later development of schizophrenia

2. To discuss critically the implications of the long latency to clinical appearance of schizophrenia for efforts at prevention and early intervention

Surgeon General's Report on Mental Health: Implications for Intervention Research

Presenter:

Howard Goldman, MD, PhD, *University of Maryland*

The objectives for this update session are:

1. To examine the rationale and process of producing a scientifically based Surgeon General's Report on Mental Health
2. To define research needs identified by the Report and implications for the clinical treatment research community

12:30 PM – 2:15 PM **Poster Session II:** *(posters will remain up until 6:00 PM)*

Afternoon Panels (Concurrent):

2:30 PM – 4:00 PM

Panel 5: NIMH Multi-site Trials in Children and Adolescents

- **The RUPP Anxiety Study: Design and Results**
  Daniel Pine, M.D., Columbia University

- **The Treatment of Adolescents with Depression Study (TADS)**
  John March, M.D., Duke University

- **The RUPP Treatment Study of Comorbid ADHD/Anxiety Disorders**
  Howard Abikoff, Ph.D., New York University

The objectives of this panel session are:

1. To examine ongoing large-scale NIMH clinical trials aimed at studying depression and attention-deficit hyperactivity disorder in children and adolescents
2. To define the special methodological considerations associated with studies of young populations, with emphasis on issues of differential diagnosis, informed consent, placebo response, and functional outcome measures

2:30 PM – 4:00 PM

Panel 6: Combination Treatments in Geriatric Psychiatry

Session Chairs: **Jacobo Mintzer, MD**, *Medical University of South Carolina*
Barry Lebowitz, PhD, *National Institute of Mental Health*

1) "**Why should cholinesterase inhibitors have an augmentation effect?"**
Presenter: Bruce Pollock, MD, Ph.D., University of Pittsburgh

2) **"Donepezil and Sertraline in the Treatment of Behavioral Disturbances associated with Alzheimer's Disease"**
Presenter: Thomas McRae, MD, Pfizer Pharmaceuticals

3) **"Atypical Antipsychotics and Cholinesterase Inhibitors in the treatment of Psychosis and Aggression in Alzheimer's Disease"**
Presenter Jacobo Mintzer, MD, Medical University of South Carolina

4) **"Donepezil in Schizophrenia and Bipolar Illness"**
Presenter: S. Craig Risch, MD, Medical University of South Carolina

Discussant: Samuel Gershon, MD, University of Pittsburgh

The objectives for this panel session are:

1. To examine the rationale for using combinations of medications in the treatment of mental disorders of the elderly, including depression and Alzheimer's Disease
2. To explain the methodological implications of using combined interventions in conducting scientifically sound treatment research, including appropriate use of medication plasma concentrations and functional as well as symptom outcome measures

2:30 PM – 4:00 PM

Panel 7: **Depression in Women across the Reproductive Cycle**

Lee Cohen, M.D., Massachusetts General Hospital
Mary Blehar, Ph.D., National Institute of Mental Health
Teri Pearlstein, Ph.D., Brown University
Zachary Stowe, M.D. Emory University

The objectives for this panel session are:

1. To describe current understanding of the pathophysiology of depressive syndromes associated with the menstrual cycle, pregnancy, and the postpartum period

2. To examine current research findings in the treatment of premenstrual dysphoric disorder and pregnancy- /postpartum-related depression, including new data on passage of antidepressant medications and active metabolites across the placenta during pregnancy and into breast milk of nursing mothers

4:15 PM – 5:45 PM

Panel 8: Clinical Development of Psychotropic Drugs: Differences and Synergies between Europe and the US

Co-Chairs: Rémy Luthringer, Ph.D., FORENAP, *Rouffach, France*
Barry Lebowitz, PhD, National Institute of Mental Health

Presenters:

Paul Bailey, M.D., FORENAP, *Rouffach, France*
Thomas Laughren, M.D., Food and Drug Administration
Herman Fuder, M.D., Robert Wood Johnson, *United Kingdom*
Rashmi Shah, M.D., *United Kingdom*
Thomas Laughren, M.D., Food and Drug Administration

The objectives for this panel are:

1. To review the medication development and drug regulatory processes, from preclinical studies and clinical trials to marketing approval, in the US and European countries
2. To critically discuss the advantages and disadvantages, to investigators, consumers, and the pharmaceutical industry, of various approaches to medication development and the drug approval process in different countries

4:15 PM – 5:45 PM

Panel 9: Why is Placebo Response So High in Clinical Trials in Depression and Panic Disorder?

Chairs: Arif Khan, MD and Mark Rapaport, MD

1. **HOW PLACEBOS WORK**
   Walter Brown, MD, Brown University

   This presentation is focused on placebos effects in all medical disorders, with special reference to Psychotropics. Potential mechanisms such as conditioning for placebo will be presented.

2. **Placebo Treated Patients in Antidepressant Clinical Trials: Symptom Reduction and Suicide Risk Using FDA Database**
Arif Khan, MD, Northwest Clinical Research Center

This presentation is focused on magnitude of change on mean total HAM-D scores among placebo treated versus antidepressant treated patients (n=8,731) as well as risk for suicide and suicide attempts (n=19, 639).

3. **Placebo Response Rates in Panic Disorder**
Mark Rapaport, MD, University of California, San Diego

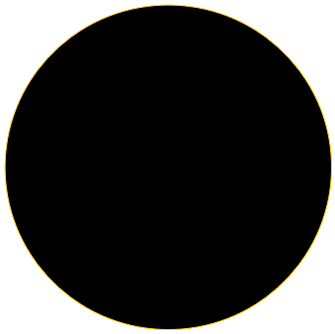
This presentation is focused on placebo response rates among Panic Disorder patients and is designed to consider alternative measures.

4. **Are We Measuring the Same Thing in Multi-Site Antidepressant Clinical Trials?**
Mark Demitrack, MD, Eli Lilly & Co

This presentation is focused on a proposal to implement a uniform method to administer HAM-D to reduce heterogeneity; in part based on results of previous clinical trials.

The objectives for this panel are:

1. To examine the incidence of placebo response in several large-scale clinical treatment trials of depression and panic disorder
2. To discuss current hypotheses regarding the mechanisms of action of placebo response in mood and anxiety disorders
3. To define the methodologic approaches to enhance the validity and reliability of symptom and functional outcome measures in clinical trials to most accurately assess treatment response



Friday, June 2

9:00 AM – 12:00 Noon **FDA Symposium**

Presenters:

Russell Katz, M.D.
Thomas Laughren, M.D.
Susan Molchan, M.D.
Roberta Glass, M.D.
Andrew Mosholder, M.D.

Objectives:

Cite current perspectives on regulatory issues in the development of drug products in following therapeutic areas: Alzheimer's disease; Premenstrual Dysphoric Disorder; Attention Deficit Hyperactivity Disorder and other psychiatric disorders in pediatric patients. Specific regulatory issues to be addressed include identification of the clinical entities, outcomes, assessment of change, trial design, and safety issues.

9:00 **Regulatory Issues in Drug Development for Cognitive Impairment In Alzheimer's Disease**
Russell Katz, MD, Food and Drug Administration

9:30 **Regulatory Issues in Drug Development for Psychiatric and Behavioral Disturbances in Alzheimer's Disease**
Thomas Laughren, MD, Food and Drug Administration

10:00 **Regulatory Issues in Drug Development for Premenstrual Dysphoric Disorder (PMDD)**
Susan Molchan, MD, Food and Drug Administration

10:30 **Regulatory Issues in Drug Development for Psychiatric Disorders in Pediatric Patients**
Roberta Glass, MD, Food and Drug Administration

11:00 **Regulatory Issues in Drug Development for Attention Deficit Hyperactivity Disorder (ADHD)**
Andrew Mosholder, MD, Food and Drug Administration

11:30 **Discussion**

Adjourn at 12:00 noon